REMARKS

This Amendment is submitted in reply to the Office Action mailed on February 24, 2005. In the Office Action, the Examiner rejected claims 13-30 and 41-87. With this Amendment, claims 13, 17-20, 22-28, 30, 50, 52, 57, 62, 64, 66-68, 70-72, 74-76, and 78-83 are amended; claims 21, 29, 41 and 63 are canceled; and new claims 84-87 are added. Upon entry of this Amendment, the above-identified application will include claims 13-20, 22-28, 30, 42-62 and 64-87.

Though claims 21, 29, 41 and 63 are canceled via this Amendment, Applicants continue to believe claims 21, 29, 41 and 63 are allowable, as originally presented in the above-identified application and also as claims 21, 29, 41 and 63 presently exist as of the present request to cancel claims 21, 29, 41 and 63. Likewise, though claims 13, 17-20, 22-28, 30, 50, 52, 57, 62, 64, 66-68, 70-72, 74-76, and 78-83 are amended via this Amendment, Applicants continue to believe claims 13, 17-20, 22-28, 30, 50, 52, 57, 62, 64, 66-68, 70-72, 74-76, and 78-83 are allowable, as originally presented in the above-identified application and as these claims presently exist as of the present request to amend these claims. Therefore, Applicants are canceling claims 21, 29, 41 and 63 and amending claims 13, 17-20, 22-28, 30, 50, 52, 57, 62, 64, 66-68, 70-72, 74-76, and 78-83 without prejudice to Applicants' right to pursue claims worded like claims 13, 17-28, 30, 41, 50, 52, 57, 62-64, 66-68, 70-72, 74-76, and 78-83, as originally presented or as worded subsequent to original presentation, in the above-identified application or in a continuation application that is based on the above-identified application.

Furthermore, no claim amendment and no claim cancellation made herein is related to any statutory patentability requirement unless expressly stated herein. Also, no claim amendment made herein is made for the purpose of limiting (narrowing) the scope of any claim.

Examiner's Objection To The Specification

In the Office Action, the Examiner objected to the specification of the above-identified application on the basis that the sequence listing information was confusing. To remedy this confusion, Applicants are submitting a revised electronic sequence listing (with an

attached paper copy) and are amending some of the specification paragraphs, as indicated above, to alter the particular sequence number referred to in these paragraphs.

Some of the primary differences between the previously submitted Sequence Listings and the presently submitted Sequence Listings are elimination of the previously provided amino acid (while retaining the previously provided nucleotide sequence) in the listing of Sequence ID No. 2, switching from the nucleotide sequence to the amino acid sequence in Sequence ID No. 4, and renumbering of the Sequence ID NOS. for the human and murine leptin sequences. The specification amendments generally consist of physically moving the Sequence ID Nos. previously given to be more closely associated with the appropriate sequence description. The only change in sequence numbers in the specification occurs with regard to the comparative murine leptin and human leptin sequence numbers. Several claims that previously recited the nucleotide sequence of Sequence ID No. 3 have been amended to instead more properly recite the nucleotide sequence of Sequence ID No. 2, which is related to Sequence ID No. 3, since Sequence ID No. 3 details an amino acid sequence, rather than the recited nucleotide sequence.

Applicants note the Examiner's concern about the discontinuous nature of the nucleotides present in the nucleotide sequence (SEQ ID NO: 2) of the coding region of the porcine leptin gene depicted in Figures 1A-1D and about the discontinuous nature of the amino acids present in the amino acid translation (SEQ ID NO: 3) of the coding region of the porcine leptin gene depicted in Figures 1A-1D. To address this concern, Applicants have amended the paragraph describing FIGS. 1A-1D to indicate Figures 1A-1D , though discontinuously, depict the ordering of nucleotides present in the nucleotide sequence (SEQ ID NO: 2) of the coding region of the porcine leptin gene and the ordering of amino acids present in the amino acid translation (SEQ ID NO: 3) of the coding region of the porcine leptin gene.

These amendments are believed to satisfactorily address the Examiner's objection to the specification. Consequently, reconsideration and withdrawal of the objection to the specification is respectfully requested.

Examiner's Objection to the Claims

In the Office Action, the Examiner objected to claims 17 and 18 under 37 C.F.R. §1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. According to the Examiner:

> The dependent claims 17-18 place size limitations on the DNA of 'at least 20' or 'at least 50' bases, which is no where near the necessary size of a DNA which will encode a porcine leptin polypeptide, absent evidence to the contrary. Therefore, the claims do not appear to further limit the claims from which they depend.

In this regard, the Examiner also stated:

> Molecules of this length would encode a fragment, and claims of this nature could be presented as independent claims or they could be presented in a different manner so as to not include the requirement that they encode "porcine adipocyte polypeptide leptin".

Applicants disagree with the Examiner's contention regarding molecule lengths needed to encode a DNA molecule and note the Examiner has not advanced any evidentiary support for the Examiner's contention. Nonetheless, Applicants have amended claims 17 and 18, as indicated above, to incorporate the Examiner's suggestion. Claims 17-18 now read as follows:

> *17. (Currently Amended) The isolated single or double-stranded DNA molecule of claim 13 wherein the isolated DNA molecule is at least about 20 bases and encodes at least a fragment of the porcine leptin polypeptide that hybridizes to the nucleotide sequence of SEQ ID NO: 1 under stringent hybridization conditions.*
>
> *18. (Currently Amended) The isolated single or double-stranded DNA molecule of claim 13 wherein the isolated DNA molecule is at least about 50 bases and encodes at least a fragment of the porcine leptin polypeptide that hybridizes to the nucleotide sequence of SEQ ID NO: 1 under stringent hybridization conditions.*

Claims 17 and 18 are believed allowable. Consequently, Applicants respectfully ask the Examiner to reconsider and withdraw the objection to claims 17-18 under 37 C.F.R. §1.75(c) and that claims 17-18 be allowed.

Next, the Examiner objected to claims 41, 46-49, 51, 54, 59, 63, 65, 69, 73, and 77 under 37 C.F.R. §1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. According to the Examiner:

> Claims 41, 46-49, 51 , 54, 59, 63, 65, 69, 73, and 77 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The recited claims and the claims from which they depend all recite language regarding encoding 'porcine adipocyte polypeptide leptin' or 'porcine leptin polypeptide' or 'porcine leptin polypeptide leptin' (see claim 76). However, the instant specification only describes a single protein of leptin which has been isolated from pigs, making it porcine leptin (Figure 2 and 3). Specifically, the specification indicates at page 3 'this invention is directed to a porcine adipocyte polypeptide (i.e., the porcine leptin protein)' and uses the terms 'porcine adipocyte polypeptide' and 'porcine leptin' interchangeably as meaning the same protein throughout the specification (see page 6 for example). Therefore, the further dependent claims which recite that the encoded protein is 'porcine leptin' is not further limiting.

In regard to Applicants' various usages of the terms "porcine adipocyte polypeptide leptin" or "porcine leptin polypeptide" or "porcine leptin polypeptide leptin" in different claims, the Examiner also stated:

> These recitations are used separately as well as in conjunction with one another as if to denote a distinction between the molecules which are encoded. However, a fair reading of the instant specification would indicate that the above recitations all refer to the same protein, which is leptin produced in pigs.

Applicants agree with the Examiner's characterization of "porcine adipocyte polypeptide leptin" or "porcine leptin polypeptide" or "porcine leptin polypeptide leptin" as each referring to porcine leptin produced in pigs, and further emphasizes the porcine leptin may be obtained from anywhere such porcine leptin may be found within the pig.

Claim 41 has been canceled, as indicated above, since claim 41 depends from claim 13 and merely repeats details recited in claim 13, which now recites "porcine leptin polypeptide," rather than "porcine adipocyte polypeptide leptin." The amendment of claim 13 to recite "porcine leptin polypeptide," rather than "porcine adipocyte polypeptide leptin," was not made for purposes of overcoming any statutory ground of rejection and instead merely acknowledges the understanding that "porcine leptin polypeptide" and "porcine adipocyte polypeptide leptin" each refer to the same thing, namely porcine leptin coming from a pig.

Also, claim 63 has been canceled, since Applicants have discovered claim 63 is a duplicate of claim 48, where both claims 48 and 63 depend from claim 25. The cancellation of claim 63 was not made for purposes of overcoming any statutory ground of rejection and instead merely acknowledges the understanding that claims 48 and 63 were duplicates of each other. Applicants' cancellation of claim 41 is in no way related to the Examiner's objection to claim 41 under 37 C.F.R. §1.75(c).

The Examiner's comments with regard to claim 46 are not understood, since claim 46 specifies the "functional derivative" encodes for porcine leptin polypeptide and depends from claim 22 that instead specifies the isolated DNA molecule encodes a porcine leptin polypeptide. Likewise, the Examiner's comments with regard to claim 47 are not understood, since claim 47 specifies the "variant" encodes for porcine leptin polypeptide and depends from claim 24 that instead specifies the isolated DNA molecule encodes a porcine leptin polypeptide. Also, the Examiner's comments with regard to claim 48 are not understood, since claim 48 specifies the "variant" encodes for porcine leptin polypeptide and depends from claim 25 that instead specifies the isolated RNA molecule encodes a porcine leptin polypeptide and further specifies the mRNA molecule may be encoded by the variant, but does not explicitly state anything about the variant encoding the porcine leptin polypeptide. Analogous comments are applicable with regard to claims 51, 54, 59, 69, 73, and 77. Due to these distinctions, it is not seen how the Examiner can maintain the stated objections to claims 46-49, 51, 54, 59, 69, 73, and 77.

Claims 46-49, 51, 54, 59, 69, 73, and 77 are allowable. Therefore, Applicants respectfully ask the Examiner to reconsider and withdraw the objection to claims 46-49, 51, 54, 59, 69, 73, and 77 under 37 C.F.R. §1.75(c) and that claims 46-49, 51, 54, 59, 69, 73, and 77 be allowed.

Claim Rejections Under the Enablement Requirement of the First Paragraph of 35 U.S.C. §112

In the Office Action, the Examiner rejected claims 13-15, 17-20, 25, 30, 41-42, 44, 50, 52, 53, 55, 57-58, 60, 62, 64, 66, 68, 70, 72, 74, 75, 78, and 80-82 under 35 U.S.C. §112, first paragraph, as allegedly failing to satisfy the enablement requirement:

> The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Despite the Examiner's comments, claims 13-15, 17-20, 25, 30, 42, 44, 50, 52, 53, 55, 57-58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80-82 are enabled by the disclosure in accordance with the first paragraph of 35 U.S.C. §112.

As indicated above, claim 41 has been canceled, since claim 41 depends from claim 13 and merely repeats details recited in claim 13. Applicants' cancellation of claim 41 is in no way related to the Examiner's rejection of claim 41 under the enablement requirement.

The dispute that is the basis of this enablement rejection centers on the meaning of the term "encode" and the ability of shorter nucleotides to encode porcine leptin. The Examiner does not challenge Applicant's contention that the application provides appropriate details explaining how to practice the present invention, as defined in claims 16, 21-24, 31-41, 43, 45-49, 51, 54, 56, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, or 83. Instead, the Examiner challenges the veracity of the statement on the basis that the Examiner believes Applicant's definition of encode is erroneous. Applicant has provided evidence to the Examiner demonstrating support for Applicant's definition of encode. See the discussion on pages 27 and 28 of the Amendment After Final filed November 23, 2004 in response to the Final Office Action dated June 3, 2004 along with the article by Y.M. Kennes, B.D. Murphy, F. Pothier and M.-F Palin, entitled Characterization of Swine *Leptin* (*Lep*) Polymorphisms and Their Association with Production Traits (2001) attached as Exhibit A of the Amendment After Final filed November 23, 2004 in response to the Final Office Action dated June 3, 2004.

The Kennes article demonstrates, despite the Examiner's allegation to the contrary, that the scientific literature does indeed recognize nucleic acid molecules having at least about 20 bases of a nucleotides sequence derived from a leptin gene that encodes a leptin molecule. The Examiner continues to allege "the art does not recognize a nucleic acid as short as 20-50 nucleotides long that encodes a leptin molecule." However, despite the fact Applicant has provided evidence in support of Applicant's understanding of the meaning of "encode," the Examiner has not yet produced any such evidence in support of the Examiner's contention that Applicant's interpretation is wrong. Since Applicant has demonstrated the specification disclosure, on its face, teaches how to make and use the

invention defined in the claims, the Examiner is obligated, under In re Wright, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993)., to back up the Examiner's assertions controverting the truth and accuracy of any enabling statements in dispute, including the meaning of "encode," with acceptable evidence or reasoning explaining why the enabling statement is believed untrue or inaccurate. The Examiner's mere allegation about what the art does not recognize, without more, is insufficient to carry the Examiner's obligation under Wright.

Claims 13-15, 17-20, 25, 30, 42, 44, 50, 52, 53, 55, 57-58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80-82 are believed allowable. Therefore, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 13-15, 17-20, 25, 30, 42, 44, 50, 52, 53, 55, 57-58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80-82 under the enablement requirement of the first paragraph of 35 U.S.C. §112 and that claims 13-15, 17-20, 25, 30, 42, 44, 50, 52, 53, 55, 57-58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80-82 be allowed.

Claim Rejections Under the Second Paragraph, 35 U.S.C. §112

In the Office Action, the Examiner rejected claims 19-30 and 41-83 under the second paragraph of 35 U.S.C. §112 as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Despite the Examiner's various comments in support of these rejections, Applicant believes claims 13-20, 22-28, 30, 42-62, and 64-83 are definite within the meaning of the second paragraph of 35 U.S.C. 112.

As indicated herein, claims 21, 29, 41, and 63 have been canceled. Claim 21 has been rewritten as new claim 86 that depends from independent claim 50; claim 21, as rewritten in the form of new claim 86, has the same or greater scope than before being rewritten. Also, claim 29 has been rewritten as new claim 87 that depends from independent claim 30; claim 29, as rewritten in the form of new claim 87, has the same or greater scope than before being rewritten. Claim 41 has been canceled, as indicated above, since claim 41 depends from claim 13 and merely repeats details recited in claim 13. Also, claim 63 has been canceled, since Applicants discovered claim 63 is a duplicate of claim 48, where both claims 48 and 63 depend from claim 25. Applicant's cancellation of claims 21, 29, 41, and 63 was not made for purposes

of overcoming any statutory ground of rejection. Furthermore, Applicants' cancellation of claims 21, 29, 41, and 63 is in no way related to the Examiner's rejection of claims 21, 29, 41, and 63 under the second paragraph of 35 U.S.C. 112.

In one aspect, the Examiner alleged the nucleotide sequence of SEQ ID NO:3 defined in claims 19-30, 46-52, 57, and 62-83 is disclosed as an amino acid sequence:

> Claims 19-30, 46-52, 57, 62, 63-83 refer to 'a nucleotide sequence of SEQ ID NO:3' (or depend from claims which recite SEQ ID NO:3). Because of the new Sequence Listing which was filed 03 December 2004, SEQ ID NO:3 is now an amino acid sequence. Since an amino acid sequence is not a nucleotide sequence, it is not clear what Applicant is claiming. Correction of the Sequence Listing and or Specification and/or claims may obviate this ground of rejection.

Despite the Examiner's allegations, claims 19-20, 22-28, 30, 46-52, 57, 62, and 64-83 are believed definite in accordance with the second paragraph of 35 U.S.C. §112. As indicated above, claims 21, 29, 41, and 63 have been canceled for a reason unrelated to the Examiner's rejection of claims 21, 29, 41, and 63 under the second paragraph of 35 U.S.C. 112.

Applicants have amended claims 19-20, 22-28, 30, 50, 52, 62, 64, 66-68, 70-72, 74-76, and 78-83 to more properly recite the nucleotide sequence of Sequence ID No. 2, which is related to the formerly recited Sequence ID No. 3, since Sequence ID No. 3 details an amino acid sequence, rather than the recited nucleotide sequence. This action does not narrow any of claims 19-20, 22-28, 30, 50, 52, 62, 64, 66-68, 70-72, 74-76, and 78-83 or any claims depending from claims 19-20, 22-28, 30, 50, 52, 62, 64, 66-68, 70-72, 74-76, and 78-83, but instead merely shifts the defined Sequence ID number from an amino acid sequence to a nucleotide sequence that corresponds to the previously recited amino acid sequence. In essence, the label (i.e. Sequence ID. NO) changed, but the substance did not change.

This action is believed to address the Examiner's concerns about the sequence listings provided in claims 19-20, 22-28, 30, 46-52, 57, 62, and 64-83, and claims 19-20, 22-28, 30, 46-52, 57, 62, and 64-83 are correspondingly believed allowable. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims -20, 22-28, 30, 46-52, 57, 62, and 64-83 under the second paragraph of 35 U.S.C. §112 and that claims -20, 22-28, 30, 46-52, 57, 62, and 64-83 be allowed.

In another aspect, the Examiner challenged Applicants' use of "a" or "an" when identifying a sequence associated with a particular sequence identification number:

> Claims 13, 19-22, 24-25, 27-28, 62, 68, 81 recite the article 'a' in place of 'the' when referring to the sequence represented by a sequence identifier. This is indefinite when referring to a single sequence because reference to a specific sequence would require the use of the article 'the'. The use of 'a' implies that there are multiple sequences to chose from or represented by the sequence identifier, which is not the case when referring to a specific sequence as one is when referencing a sequence identifier.

Despite the Examiner's allegations, claims 13, 19-20, 22, 24-25, 27-28, 62, 68, and 81 are believed definite in accordance with the second paragraph of 35 U.S.C. §112. As indicated above, claim 21 has been canceled for a reason unrelated to the Examiner's rejection of claim 21 under the second paragraph of 35 U.S.C. 112.

Applicants included the article "a" or "an" in place of "the" to provide antecedent basis pursuant to §2173.05(e) of the Manual of Patent Examining Procedure (MPEP) , Rev. May, 2004. However, at the Examiner's suggestion, Applicants have substituted the article "the" in claims 13, 19-20, 22, 24-25, 27-28, 62, 68, and 81, since Applicants intended to refer to only one sequence, with the understanding the molecule that is hybridizing need not necessarily hybridize to the full extent of the recited sequence. Claims 13, 24, 25, 27-30, 43, and 45 are believed allowable. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 13, 19-20, 22, 24-25, 27-28, 62, 68, and 81 under the second paragraph of 35 U.S.C. §112 and that claims 13, 19-20, 22, 24-25, 27-28, 62, 68, and 81 be allowed.

In another aspect, the Examiner alleged Applicants' use of "at least about" to characterize the number of bases (length) of a molecule in claims 17 and 18 and to characterize the number of bases of a sequence to which a molecule hybridizes in claims 14, 15, 19, 20, 44, 52, 55, 57, 60, 62, 64, 66, 70, 74, 78, 80, 82 is indefinite. In support of this rejection, the Examiner alleged:

> Claims 14, 15, 17, 18, 19, 20, 44, 52, 55, 57, 60, 62, 64, 66, 70, 74, 78, 80, 82 are indefinite for the recitation 'at least about' in conjunction with a number of nucleotides which are to hybridize. This recitation is indefinite because the lower limits of what are to be encompassed by the claims is not clear. The instant specification does not indicate what range 'at least about' is meant to encompass. Furthermore, 'at least' is in direct conflict with 'about' since 'at least' sets a lower limit to the range, but 'about' changes that limit. Therefore, the claims are indefinite because the metes and bounds of 'at least about' cannot be determined.

Despite the Examiner's allegations, claims, 14, 15, 17, 18, 19, 20, 44, 52, 55, 57, 60, 62, 64, 66, 70, 74, 78, 80, 82 are believed definite in accordance with the second paragraph of 35 U.S.C. §112.

The Examiner suggests via a semantics exercise that one reads this as a two part phrase and first decides what range is set by the term "at least" and then would be confused about how to employ the final "about" term." However, this argument is clearly invalid, since the term "at least about X" could alternatively be written as "about X or more." Clearly, no one of ordinary skill in the art would be confused about the meaning of "at least about X" following this straightforward illustration.

Furthermore, rather than the extent of the range, the Examiner's initial comment illustrates the Examiner believes one of ordinary skill in the art would be instead merely be confused about the lower end starting point of the stated range. The issue then comes down to whether one of ordinary skill in the art would understand the meaning of "about 20" or "about 50." Applicants assert such use of about to allow minor variations from the base number (20 or 50 under the present facts) is commonplace in patent drafting, and the Examiner has not stated adequate facts to demonstrate the existence of any real ambiguity. Applicants see no basis for believing one of ordinary skill in the art would not reasonably be able to determine the scope of the terminology at issue. The Examiner certainly has not stated any hypothetical facts illustrating or demonstrating that an unreasonably ambiguous situation exists here under the facts of the present application.

Claims 14, 15, 17, 18, 19, 20, 44, 52, 55, 57, 60, 62, 64, 66, 70, 74, 78, 80, 82 are believed allowable. Therefore, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 14, 15, 17, 18, 19, 20, 44, 52, 55, 57, 60, 62, 64, 66, 70, 74, 78,

80, 82 under the second paragraph of 35 U.S.C. §112 and that claims 14, 15, 17, 18, 19, 20, 44, 52, 55, 57, 60, 62, 64, 66, 70, 74, 78, 80, 82 be allowed.

In yet another aspect, the Examiner alleged Applicants' use of three different phrases amounts to use of three different names for the same thing:

> Claims 13-30 and 41-83 are indefinite for the use of 'porcine adipocyte polypeptide leptin' or 'porcine leptin polypeptide' or 'porcine leptin polypeptide leptin' (dependent claims are included as well, even if they do not explicitly recite the noted language). These recitations are used separately as well as in conjunction with one another as if to denote a distinction between the molecules which are encoded. However, a fair reading of the instant specification would indicate that the above recitations all refer to the same protein, which is leptin produced in pigs. Only a single protein is disclosed in the instant specification (with and without signal sequence; SEQ ID NO:3 and 6) and there is no disclosure to distinguish one recitation from another. Therefore, the use of these recitations as limitations in the claims is vague and indefinite because the cation discloses that they are the same protein as evidenced by the disclosure at page 6. The metes and bounds of what is being claimed cannot be determined because no differences can be ascertained for the different recitations which appear to mean the same thing.

Despite the Examiner's allegations, Applicants do not believe Applicants' variable usage of "porcine adipocyte polypeptide leptin" or "porcine leptin polypeptide" or "porcine leptin polypeptide leptin" renders any claim of claims 13-20, 22-28, 30, 42-62, and 64-83 indefinite under the second paragraph of 35 U.S.C. §112. As indicated above, claims 21, 29, 41, and 63 have been canceled for reasons unrelated to the Examiner's rejection of claims 21, 29, 41, and 63 under the second paragraph of 35 U.S.C. 112.

Nonetheless, Applicants agree with the Examiner's characterization of "porcine adipocyte polypeptide leptin" or "porcine leptin polypeptide" or "porcine leptin polypeptide leptin" as each referring to porcine leptin produced in pigs, and further emphasizes the porcine leptin may be obtained from anywhere such porcine leptin may be found within the pig. Consequently, to satisfy the Examiner's desire for use of common terminology, and not for purposes of addressing the present indefiniteness rejection under the second paragraph of 35 U.S.C. §112, Applicants have amended claims 13, 22, 24-25, 27-28, 30, 50, and 76 so that claims 13-20, 22-28, 30, 42-62, and 64-83 all now recite porcine leptin polypeptide

Claims 13-20, 22-28, 30, 42-62, and 64-83 are each believed allowable. Therefore, Applicants respectfully ask the Examiner to reconsider and withdraw the rejection of claims 13-20, 22-28, 30, 42-62, and 64-83 under the second paragraph of 35 U.S.C. §112 and that claims 13-20, 22-28, 30, 42-62, and 64-83 each be allowed.

Next, the Examiner stated that Applicants' use of the term "stringent hybridization conditions" in various claims allegedly renders claims 13-30 and 41-83 indefinite:

> Claims 13-30 and 41-83 are indefinite for the limitation of 'stringent hybridization conditions'. The limitation 'stringent hybridization conditions' is equivalent to reciting a range without indicating the metes and bounds of the conditions since there is no indication of what conditions are to be encompassed by the claims. The specification does not provide a definition of what conditions are considered 'stringent' and the art recognizes a multitude of conditions which could be used and considered 'stringent'.. . . . Hybridization conditions are found in the specification in conjunction with Example II, however, the specification does not disclose that these conditions are what is intended by the recitation of 'stringent hybridization conditions'.

Despite the Examiner's allegations, Applicants do not believe use of the "stringent hybridization" terminology renders any claim of claims 13-20, 22-28, 30, 42-62, and 64-83 indefinite under the second paragraph of 35 U.S.C. §112. As indicated above, claims 21, 29, 41, and 63 have been canceled for reasons unrelated to the Examiner's rejection of claims 21, 29, 41, and 63 under the second paragraph of 35 U.S.C. 112.

Though the term "stringent hybridization conditions" may be broad and encompass a wide variety of complementary or individually sufficient conditions; however, mere use of broad terminology does not render a claim indefinite. The question is whether one of ordinary skill in the art would understand what is meant by stringent hybridization conditions. In this regard, a hard and fast definition is unnecessary if those of ordinary skill in the art would understand what is meant by stringent hybridization conditions.

The Examiner acknowledges that there are many routes to attaining stringent hybridization conditions:

> . . . there are a multitude of conditions which the prior art and those skilled in the art recognize as being 'stringent hybridization conditions'. Varying the length of the probe, the temperature at which the hybridization occurs, the salt

> concentration at various stages including wash steps and varying denaturing agents can all provide different specificities in hybridization. Without knowing which conditions are intended by the claims, the metes and bounds of those molecules which are encompassed by the claims cannot be determined.
>
> . . .
>
> However, in the absence of a true definition in the specification that indicates what conditions are intended by 'stringent', the reason is maintained as it is clearly supported by Applicant's own arguments and the Declaration filed that there are a number of variables involved in hybridization, and, therefore, a number of different conditions which would provide for 'stringent' hybridization.

However, the mere fact that there are alternative approaches to attaining stringent hybridization conditions does not demonstrate any confusion about the meaning of the "stringent hybridization" terminology. It instead merely demonstrates one of ordinary skill in the art has different options for attaining stringent hybridization conditions. The Examiner's demonstration that there are plenty of alternative approaches to attaining "stringent hybridization conditions" does not support the Examiner's contention that the "stringent hybridization terminology" is confusing or indefinite. The fact that there are alternatives does not show the existence of confusion. Indeed, the Examiner produces no evidence showing one of ordinary skill in the art would be confused about the meaning of the "stringent hybridization conditions" terminology.

The Examiner alleges, or at least implies, Applicants' use of the "stringent hybridization conditions" terminology amounts to reading specification details into the claims:

> Applicant makes many references to the conditions in Examples II and III, however, limitations from the specification cannot be read into the claims Applicant may wish to include the conditions which are exemplified in Examples II and III into the claims in order to avoid the rejection of record.

However, the mere fact that one of ordinary skill in the art may look to the specification for some alternative approaches to attaining stringent hybridization conditions beyond conditions they are accustomed to using does not render the "stringent hybridization condition" terminology indefinite. Furthermore, the "stringent hybridization terminology" does not require one of ordinary skill in the art to use any of the alternative approaches described in the specification.

Finally, the Examiner alleged the Declaration Under 37 CFR 1.132 filed on December 3, 2004 was insufficient to overcome the indefiniteness rejection stated in the June 3, 2004 Office Action:

> Applicant argues this rejection beginning at page 35 of the response through page 46 of the response. The Declaration under 37 CFR 1.132 filed 03 December 2004 is insufficient to overcome the rejection of claims 13-30 and 41-83 based upon indefiniteness as set forth in the last Office action because: the Declaration and the arguments which accompany it demonstrate that there are a multitude of conditions which the prior art and those skilled in the art recognize as being 'stringent hybridization conditions'.

Applicant notes the Declaration referenced by the Examiner was merely included to demonstrate the specification of the above-identified application, based on the understanding of hybridization stringency at the time the priority application was filed, provides ample support for the 'stringent hybridization conditions" terminology recited in the claims.

The Examiner reaches an erroneous conclusion about some discussion included in the present application regarding stringent hybridization conditions:

> Page 10 of the specification makes reference to hybridization that '[I]n order to achieve higher specificity of hybridization, characterized by the absence of hybridization to sequences other than those encoding the polypeptide or a functional derivative thereof, a length of at least about 50 nucleotides is preferred'. Based on this language, it would seem that claims that include the limitation of 'at least about 20 nucleotides' would be in direct conflict with the limitation that 'stringent hybridization conditions' are used. Hybridization conditions are found in the specification in conjunction with Example II, however, the specification does not disclose that these conditions are what is intended by the recitation of 'stringent hybridization conditions'.

The statements cited by the Examiner are <u>not</u> in direct conflict with each other, despite the Examiner's contention to the contrary. First, Applicants note the "at least about 50 nucleotides" characterization is preferred, <u>and</u> <u>not</u> required. Certainly, the Examiner is aware that varying (increasing) the length of the probe is one approach to enhancing stringency of hybridization conditions, since the Examiner mentioned "[v]arying the length of the probe" as one way of varying hybridization stringency later at the bottom of page 12 of the present Office Action. Certainly, the Examiner recognizes that approaches other than probe length variation may be

taken to enhance hybridization stringency. This demonstrates the limitation of "at least about 20 nucleotides" is not "in direct conflict with the limitation that 'stringent hybridization conditions' are used."

Though the term "stringent hybridization conditions" may be broad and encompass a wide variety of complementary or individually sufficient conditions, the use of broad terminology does not necessarily render a claim indefinite. The Examiner acknowledges there are many routes to attaining stringent hybridization conditions. But as explained above, the mere fact that there are alternatives does not demonstrate the underlying terminology is indefinite. Despite the Examiner's many allegations and contentions, the Examiner produces no evidence showing one of ordinary skill in the art would be confused about the meaning of the "stringent hybridization conditions" terminology and therefore fails to establish the "stringent hybridization conditions" terminology is indefinite.

Claims 13-20, 22-28, 30, 42-62, and 64-83 are each believed allowable. Therefore, Applicants respectfully ask the Examiner to reconsider and withdraw the rejection of claims 13-20, 22-28, 30, 42-62, and 64-83 under the second paragraph of 35 U.S.C. §112 and that claims 13-20, 22-28, 30, 42-62, and 64-83 be allowed.

Finally, the Examiner persists with the allegation that use of the "substantially all" terminology in claims 16, 21, 23-24, 26-29, 45, 56, 61, 67, 71, 75, 79, and 83 renders claims 16, 21, 23-24, 26-29, 45, 56, 61, 67, 71, 75, 79, and 83 indefinite:

> Claims 16, 21, 23-24, 26-29, 45, 56, 61, 67, 71, 75, 79 and 83 are directed to nucleic acid molecules (DNA, mRNA) which 'hybridizes' to 'substantially all' of the bases of a recited sequence. However, these claims are indefinite for the failure to indicate what is intended by the recitation 'substantially all'.

Despite the Examiner's allegations, Applicants disagrees that use of the "substantially all" terminology automatically renders claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 indefinite under the second paragraph of 35 U.S.C. §112. As indicated above, claims 21, 29, 41, and 63 have been canceled for reasons unrelated to the Examiner's rejection of claims 21, 29, 41, and 63 under the second paragraph of 35 U.S.C. 112.

In response to Applicants' notation that applications handled by the Examiner have issued into U.S. patents with claims that employ "substantially all" terminology:

> For example, claim 1 of U.S. Patent No. 6,756,484 employs the "substantially all" terminology more than five different times. In one instance, claim 1 recites:
>
> > (C) . . . with a sufficient quantity of a first cation exchange elution buffer, which has a sufficiently high pH or ionic strength to displace **substantially all** of said authentic and non-authentic IGF-I from said cation exchange matrix . . . .
>
> Emphasis added. Applicant's review of U.S. Patent No. 6,756,484 did not identify any particular numeric meaning or degree of identity for this use of the "substantially all" terminology.

In response, the Examiner merely stated that "each application is examined on its own merits" and "[t]he facts surrounding the issued patent are not the same and are not applicable to the instant application." This is an unsatisfactory response because the Examiner failed to explain why the facts of U.S. Patent No. 6,756,484 would allow use of "substantially all" terminology in the claims without identifying any particular numeric meaning or degree of identity for this use of the "substantially all" terminology, whereas the Examiner now demands identification of a particular numeric meaning or degree of identity in order to allow Applicant's use of the "substantially all" terminology. Further explanation for this distinction between the facts pertaining to U.S. Patent No. 6,756,484 versus the facts of the present application that would support the differential treatment sought by the Examiner is respectfully requested.

The Courts do not require that any particular numeric meaning be provided for a claim containing the "substantially all" terminology to be definite. The Examiner asks "what degree of identity is intended" for Applicant's use of the "substantially all" terminology in the claims at issue. However, like numeric meaning, the Courts do not require that any "degree of identity" be provided for a claim containing the "substantially all" terminology to be definite. Rather, the question is whether those skilled in the art will be able to understand with a *reasonable* degree of accuracy what subject matter is circumscribed by the invention that is defined by a particular claim, such as claim 16. Also, the issue is not whether the particular terminology is definite, but rather whether the meaning of the claim containing the terminology

at issue is definite. The remaining argument provided in the Amendment After Final filed on December 3, 2004 is hereby incorporated by reference. The comments provided therein are thought to adequately address the Examiner's current comments on pages 13-14 of the present Office Action regarding the rejection of claims containing the "substantially all" terminology. Furthermore, as explained above, the Examiner's contentions about the "stringent hybridization terminology" being indefinite are unsupported and erroneous.

The foregoing comments along with the comments referred to in the Amendment After Final filed December 3, 2004 demonstrate one of ordinary skill in the art of microbiology would be able to understand, with a *reasonable* degree of accuracy, what subject matter is circumscribed by the invention defined by claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 which employ the "substantially all" terminology. First, the meaning of the term "substantially all" clearly means something less than "all," yet more than "half." Beyond this, the "under stringent hybridization conditions" terminology of claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 provide ample further guidance. Specifically, one of ordinary skill in the art would understand the "substantially all" term of claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 characterizes the high ("perfect or near perfect") degree to which the DNA probe base-pairs to the target DNA molecule.

Claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 are believed allowable. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 under the second paragraph of 35 U.S.C. §112 and that claims 16, 23-24, 26-28, 45, 56, 61, 67, 71, 75, 79, and 83 be allowed.

Claim Rejections Under 35 U.S.C. §103(a) Based On The Friedman Patent

In the Office Action, the Examiner continues to reject claims 21-28 and 42-83 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent N. 6,309,853 to Friedman et al. (subsequently referred to as the "Friedman patent"). In support of this rejection, the Examiner now states:

> The instant specification defines a functional derivative as
>
> Any 'fragment', 'variant', 'analog', or 'chemical derivative' of the porcine adipocyte polypeptide that retains at least a portion of the function of the porcine adipocyte polypeptide which permits its utility in accordance with the present invention. (page 9 of the specification)
>
> The instant claims are directed to isolated nucleic acids which encode porcine leptin or a 'functional derivative thereof' or 'variant thereof'. The prior art of Friedman et al. (U.S. Pat. No. 6,309,853) disclose nucleic acids which encode human and mouse leptin, which would be considered functional derivatives and/or variants of the disclosed porcine leptin since they encode leptin molecules and would possess similar functional properties as those of the porcine leptin, absent evidence to the contrary. Friedman et al. teach that the leptin gene (or OB) could be isolated from domestic animals using the methods disclosed therein (see column 26, line 53 to column 27, line 49). Friedman et al. specifically mention swine as a domestic animal for which leptin would be useful (see column 48, lines 41-57). Friedman et al. do not specifically disclose an isolated nucleic acid encoding a porcine leptin polypeptide. However, it would have been obvious to use the nucleic acid of Friedman at al. encoding human or mouse leptin and hybridize it to a porcine cDNA library and isolate a nucleic acid molecule encoding porcine leptin because Friedman at al. teach methods for isolating leptin encoding nucleic acids and also teach that it would be beneficial to administer leptin to swine. It would also have been prima facie obvious to use the nucleic acid of Friedman at al. encoding human or mouse leptin and hybridize it to porcine genomic DNA to isolate the gene encoding porcine leptin because it would have been beneficial to more completely understand the gene structure of porcine leptin. It also would have bean prima facie obvious to use the nucleic acid of Friedman at al. encoding human or mouse leptin and hybridize it to porcine mRNA to isolate the mRNA encoding porcine leptin for the benefit of understanding the nature of porcine leptin expression. Therefore, the invention as a whole would have been obvious at the time it was made, absent evidence to the contrary.

Despite the Examiner's allegations, the Friedman patent does not teach, suggest, disclose, or make obvious the invention of the above-identified application, as defined in claims 22-28, 42-62, and 64-83. As indicated above, claim 21 has been canceled for reasons unrelated to the Examiner's rejection of claim 21 under 35 U.S.C. 103(a) based upon the Friedman patent.

As noted above, the Friedman patent does not teach, suggest, or disclose the invention of the above-identified application, as defined in claims 22-28, 42-62, and 64-83. Consistent with the Examiner's observation, the Friedman patent does disclose murine and

human leptin DNA sequences and polypeptides. Also, consistent with the Examiner's observation, the Friedman patent does not disclose any porcine leptin DNA (or mRNA) molecules or polypeptides. Furthermore, consistent with the Examiner's observation, the Friedman patent does not disclose any functional derivative or variant DNA (or mRNA) molecules that encode for porcine leptin polypeptide.

For example, when recombinant porcine leptin protein is administered by intracerebroventricular (ICV) injection to crossbred prepuberal gilts (normal female pigs), the crossbred prepuberal gilts exhibit increased growth hormone secretion after the leptin administration. On the other hand, when recombinant human leptin protein is administered by ICV injection to normal male rats, the normal male rats do not exhibit increased growth hormone secretion after the leptin administration. Based on the documented differences in growth hormone secretion after ICV administration to normal fed pigs (per the previously cited Barb publication) versus normal fed rats (per the previously cited Carro publication), it is evident that recombinant porcine leptin protein surprisingly functions very differently from recombinant human leptin protein upon administration to mammals.

As another example, when recombinant porcine leptin is administered by intracerebroventricular (ICV) injection to crossbred prepuberal gilts (normal female pigs), the recombinant porcine leptin administration fails to change thyroxine (T_4) secretion. On the other hand, when recombinant mouse leptin is administered by ICV injection to normal ad libitum fed male rats, the normal ad libitum fed male rats exhibit significantly decreased thyroxine (T_4) levels in the blood after the recombinant mouse leptin administration. Since recombinant porcine leptin administration fails to change thyroxine (T_4) secretion in pigs, while recombinant murine leptin administration significantly decreased thyroxine (T_4) levels in the blood of male rats, the effects of porcine leptin administration and murine leptin administration differ dramatically, and it is evident the porcine leptin functions very differently from the murine leptin upon administration to mammals.

The Examiner suggests the Friedman patent "discloses nucleic acids which encode human and mouse leptin, which would be considered functional derivatives and/or variants of the disclosed porcine leptin since they encode leptin molecules and would possess

similar functional properties as those of the porcine leptin, absent evidence to the contrary." Applicants have provided such evidence demonstrating that Friedman nucleic acids which encode human and mouse leptin do not possess similar functional properties as the properties of porcine leptin. This evidence is summarized in the previous two paragraphs of this Amendment. Applicants' factual evidence illustrates the human leptin disclosed in the Friedman patent does not, despite the Examiner's contentions to the contrary, necessarily, or actually, possess functional properties similar to the functional properties of the porcine leptin disclosed in the above-identified application. Nonetheless, in response to this presentation of differing properties, the Examiner switched horses and basically alleged Applicants could only consider functional properties disclosed for porcine leptin in the present application.

This is an erroneous and overly restrictive view by the examiner. The evidence Applicants have already presented demonstrates functional differences between the Freidman leptin and porcine leptin. The fact that those differences exist with some functional attributes raises serious doubts about the correspondence in other functional attributes, such as those disclosed in the present application, despite the Examiner's attempt to avoid this evidence. Consequently, it is clear Applicant has rebutted the Examiner's prima facie case of obviousness and it is the Examiner's obligation to now withdraw the present rejection or present contrary evidence demonstrating correspondence in other functional attributes between the Freidman leptin and porcine leptin.

Furthermore, the Examiner relies on purely conclusory argument in support of the alleged obviousness of creating the porcine invention of the present application based on the disclosure of the Friedman patent. Specifically, the Examiner relies on blue sky "knowledge base" enhancements the Examiner pulls out of thin air as the alleged grounds for attempting to hybridize human or murine leptin to porcine DNA:

> It would also have been prima facie obvious to use the nucleic acid of Friedman at al. encoding human or mouse leptin and hybridize it to porcine genomic DNA to isolate the gene encoding porcine leptin because it would have been beneficial to more completely understand the gene structure of porcine leptin. It also would have bean prima facie obvious to use the nucleic acid of Friedman at al. encoding human or mouse leptin and hybridize it to porcine mRNA to isolate the mRNA encoding porcine leptin for the benefit of understanding the nature of porcine leptin expression.

Thus, the "suggestion" comes from the mind of the Examiner, rather than as any real and tangible suggestion provided by the art. Such suggestions developed in the absence of corroboration by the art are suspect. Such suggestions developed in the absence of corroboration by the art are particularly useful when attempting to support an obviousness allegation that is in fact based on hindsight reconstruction. Generalized "knowledge base" enhancement necessarily must fail as a basis for obviousness since success of such a basis, when aimed in any direction about the art, would bring invention to a halt and to the knees of the Friedman patent. This is true, because one could always dream up some nice potential use for the enhancing the general knowledge base, once it was known what target one is trying to bring to a halt.

Continuing, based on the factual results noted above and despite the Examiner's contentions to the contrary, the Examiner's speculative suggested hybridization of the nucleic acid of the Friedman patent that encodes murine leptin to a porcine DNA library and subsequent isolation of a nucleic acid molecule encoding porcine leptin is not suggested for yet another reason. Specifically, based on the known differences between functional attributes of porcine leptin and murine leptin, one of ordinary skill in the art would not expect the functional characteristics of the murine leptin disclosed in the Friedman patent would be helpful for confirming isolation of a nucleic acid molecule encoding for porcine leptin, as claimed in the above-identified application. This demonstrated lack of correspondence between functional properties of murine leptin versus porcine leptin would instead suggest that such a project would not be advisable. Analogous reasoning applies with regard to human leptin, since the differences in functional characteristics of the human leptin disclosed in the Friedman patent versus the functional characteristics of the porcine leptin of the present invention would not support confirmation of isolation of a nucleic acid molecule encoding for porcine leptin, as claimed in the above-identified application.

Claims 22-28, 42-62, and 64-83 are believed allowable. Consequently, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of claims 22-28, 42-62, and 64-83 under 35 U.S.C.§103(a) based on the Friedman patent and that pending claims 22-28, 42-62, and 64-83 be allowed.

Specification Amendment By Applicants

Applicants have amended the specification, at page 25, line 16, through page 26, line 1, to update the address of the American Type Culture Collection, which has changed since the above-identified application was filed. No new matter is added by this amendment. Entry of this amendment is therefore respectfully requested.

New Claims Added by Applicants

Applicants have added new claims 84-87. New claims 84-87 do not add any new matter to the above-identified application. Support for new claims 84-87 is believed to exist throughout the above-identified application. Applicants respectfully request consideration and allowance of new claims 84-87.

CONCLUSION

Claims 13-20, 22-28, 30, 42-62, and 64-87 are believed allowable. Therefore, reconsideration and allowance of claims 13-20, 22-28, 30, 42-62, and 64-83 is respectfully requested. Likewise, consideration and allowance of new claims 84-87 is respectfully requested. The Examiner is invited to contact Applicants' below-named attorney, Philip F. Fox, to facilitate allowance of the above-identified application.

Respectfully submitted,

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